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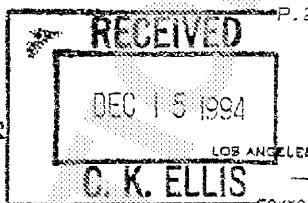
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December 14, 1994

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VIA FEDERAL EXPRESS AND COURIER

Cathy Ellis, Ph.D.
Richard Allan Carchman, Ph.D.
Philip Morris U.S.A.
Research Center
P.O. Box 26583
Richmond, Virginia 23261-6583

Dear Cathy and Richard:

Today Peter Grossi and I spoke with Richard after failing to reach Cathy. We discussed the status of our smoking cessation-threshold project. We (Arnold & Porter) plan to draft a 10-20 page document setting forth our analysis of, and conclusions from, the literature on nicotine intake and its relationship, if any, to successful smoking cessation. Specifically, we intend to concentrate on cotinine as a biomarker for nicotine intake and the eight studies we found which attempt to examine cotinine levels and their relationship to smoking cessation.

Our view and analysis will be set forth in the context of the nicotine threshold theories and proposals outlined and discussed in recent months. In order to better structure our arguments, we hope to rely on your scientific expertise and familiarity with these issues. Enclosed are the eight identified cotinine articles. As you review them, you may have a variety of thoughts, criticisms, and comments useful to us. In addition to comments concerning the statistics, pharmacologic, and other scientific observations related to the eight studies, below I list some general areas of interest on which your thoughts would be most useful:

1. Use of cotinine as a biomarker-predictor of smoking cessation success (advantages, disadvantages, problems).

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2. Use of cotinine as a biomarker for determining nicotine "addiction," dependence, or simply intake.
 - a. Is plasma cotinine a reliable, validated method to measure nicotine intake?
 - b. Do models other than "addiction" better explain smoking behavior?
 - c. Does nicotine replacement reliably reflect smoking behavior and/or cravings for nicotine?
 - d. Are specific nicotine levels associated with addictive-type behaviors or effects?
 - e. Is there any known correlation between plasma cotinine levels and central nervous system nicotine or cotinine levels?
3. The Benowitz and Henningfield NEJM article and proposal.

As always, your assistance is greatly appreciated. I look forward to seeing you both again sometime soon.

Sincerely,



David L. Katz

Enclosures

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